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<b>(21) International Application Number:</b> PCT/US98/13600 <b>(22) International Filing Date:</b> 30 June 1998 (30.06.98) <b>(71) Applicant:</b> AVON PRODUCTS, INC. [US/US]; 1251 Avenue of the Americas, New York, NY 10020-1196 (US). <b>(72) Inventors:</b> KYROU, Christos, D.; Apt. 80, Parkside Drive, Suffern, NY 10901 (US). MARTIN, Dennis, M.; 8 Tenney Lane, Cornwall, NY 12518 (US). SIMPSON, Susan, E.; 349 Wyckoff Avenue, Wyckoff, NJ 07841 (US). TEAL, Janice, J.; 40 Forest Avenue, Old Greenwich, CT 06870 (US). <b>(74) Agent:</b> RUGGIERO, Charles, N., J.; Ohlandt, Greeley, Ruggiero & Perle, L.L.P., 9th floor, One Landmark Square, Stamford, CT 06901-2682 (US).		<b>(81) Designated States:</b> CN, ID, JP.  <b>Published</b> <i>With international search report.</i>
<b>(54) Title:</b> SKIN WHITENING COMPOSITION  <b>(57) Abstract</b> <p>The composition has a skin whitening blend. The skin whitening blend has a hypopigmenting component and an antioxidant. The skin whitening blend may also have a component responsible for enhancing or accelerating the skin cell turnover rate that is selected from the group consisting of: lactic acid; glycolic acid; a mixture of lactic acid and glycolic acid; and a blend of lactic acid, malic acid and citric acid. The skin whitening blend may also comprise the hypopigmenting component, the antioxidant and a sunscreen, and the accelerant component.</p>		

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## **SKIN WHITENING COMPOSITION**

### **FIELD OF THE INVENTION**

The present invention relates to a novel skin whitening blend that is  
5 a synergistic combination of a hypopigmenting component and an  
antioxidant. The skin whitening blend is further incorporated into a suitable  
topical vehicle to provide a skin whitening composition. Optionally, the  
novel skin whitening blend may also incorporate a sunscreen and an  
accelerant.

10

### **OBJECTS OF THE INVENTION**

It is an object of the present invention to provide an efficacious skin  
whitening blend that includes a hypopigmenting component and an  
antioxidant.

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It is another object of the present invention to provide such an  
efficacious skin whitening blend that further comprises a sunscreen.

20

It is yet another object of the present invention to provide such an  
efficacious skin whitening blend that further comprises either lactic acid,  
glycolic acid, or a combination thereof, or a blend of lactic acid, malic acid  
and citric acid.

It is still another object of the present invention to provide such an  
efficacious skin whitening blend that further comprises both a sunscreen  
and an accelerant.

It is a further object of the present invention to provide an efficacious skin whitening composition that is the skin whitening blend of the present invention in a pharmaceutically elegant topical vehicle.

It is a still further object of the present invention to provide an  
5 efficacious skin whitening composition that is a cream.

It is yet a further object of the present invention to provide an efficacious skin whitening composition that may be incorporated into a lotion, solution, hydroalcoholic liquid, powder, pack or dermal patch.

## 10 DESCRIPTION OF THE PREFERRED EMBODIMENTS

The present invention relates to a skin whitening blend (hereinafter "skin whitening blend") that is incorporated into a suitable topical vehicle to comprise the total skin whitening composition of the present invention. Unless otherwise defined, all percentages disclosed herein are weight  
15 percentages of the total skin whitening composition (hereinafter "composition").

Suitable topical vehicles that may be used with the present invention include cream, lotion, solution, hydroalcoholic liquid, pack, powder and dermal patch.

20 The activity/efficacy of the composition is defined herein as lightening of skin color, evening of skin tone/color, reduction in the appearance of solar lentigines (age spots) or ephilides (freckles), reduction of melasma, reduction of chloasma, reduction of post-inflammatory

hyperpigmentation, reduction of pigmented keratoses, and/or the reduction of any sun-induced damage.

The first embodiment of the present invention is a composition having a skin whitening blend. The skin whitening blend has a  
5 hypopigmenting component and an antioxidant. In a second embodiment of the present invention, the skin whitening blend also has a component enhances or accelerates the skin cell turnover rate (hereinafter "accelerant"). In a third embodiment of the present invention, the skin whitening blend has the hypopigmenting component, the antioxidant and a  
10 sunscreen. A fourth embodiment of the present invention has a hypopigmenting component, an antioxidant, a sunscreen and an accelerant.

The hypopigmenting component for all four embodiments includes one of the following constituents: (i) a licorice extract; (ii) a natural extract  
15 that includes at least one of the following extracts: hamamelitannin (Hamamelis virginiana) extract, bearberry (Arctostaphylos uva ursi), bilberry (Vaccinium myrtillus), chlorella (Chlorella vulgaris), cowberry (Vaccinium vitis idaea), grape, molasses (Black sugar), mulberry, saxifraga and scutellaria, pear, guava, or a mixture thereof; and (iii) a blend of the  
20 licorice extract as defined in (i) and a natural extract blend as defined in (ii) (hereinafter "natural extract blend"). Preferably, at least a portion of either the mulberry extract or the scutellaria extract is derived from the root of the respective plant.

It is preferred that the hypopigmenting component is the licorice extract (i). The more preferred hypopigmenting component for the composition is the natural extract blend (iii), (which includes both the licorice extract (i) and the natural extract (ii)). However, it is even more preferred that the hypopigmenting component is the combination of the more preferred embodiment of the licorice extract (i) and the more preferred first embodiment of the natural extract mixture (ii). It is most preferred that the hypopigmenting component is the combination of the most preferred embodiment of licorice extract (i) and the most preferred first embodiment of the natural extract mixture (ii).

When the hypopigmenting component has a licorice extract, as in either (i) or (iii) set forth above, either a water soluble (or aqueous) or an oil soluble licorice extract may be used.

Examples of suitable water soluble licorice extracts are glycolic licorice extracts, alcoholic licorice extracts, and combinations thereof. If a water soluble licorice extract is used, the concentration of the licorice extract is greater than about 0.001 wt% to about 30 wt%.

An oil soluble licorice extract is the preferred licorice extract. Preferably, the oil soluble licorice extract is in powder form and is from about 0.001 wt% to about 5.0 wt%, more preferably from about 0.002 wt% to about 1.0 wt%, of the composition. It is even more preferable that the oil soluble licorice is from about 0.002 wt% to about 0.2 wt% of the composition. It is most preferable that the oil soluble composition is about 0.05 wt% to about 0.1 wt% of the composition. The oil soluble licorice

extract may have one or more of the following constituents: glabridin, glabrene, formononetin, glabrol and other related phenolic compounds. Examples of phenolic compounds may include hispaglabridin-A, 4'-O-methylglabridin, and 3'-hydroxy-4'-O-methylglabridin.

5           With regard to the natural extract (ii), any natural extract has hypopigmenting activity if used alone. However, to achieve the level of lightening of skin tone that is desired by applicants, it is preferred that the natural extract be a mixture of at least two extracts selected from the following group: bearberry, bilberry, chlorella, cowberry, grape, guava, 10 hamamelitannin, molasses, mulberry, pear, saxifraga and scutellaria (hereinafter "natural extract mixture"). For example, in a first such preferred embodiment, the natural extract mixture has both pear and guava extracts. In a second preferred embodiment, the natural extract mixture has bearberry, chlorella, grape, hamamelitannin, molasses, 15 mulberry, saxifraga and scutellaria extracts. In a third such preferred embodiment, the natural extract mixture has all of the following extracts: bearberry, grape, hamamelitannin, mulberry, saxifraga and scutellaria. In a fourth such preferred embodiment, the natural extract mixture has all of the following extracts: bearberry, bilberry, chlorella, cowberry, grape, 20 hamamelitannin, molasses, mulberry, saxifraga, scutellaria, pear and guava.

          If the hypopigmenting component is the mixture of natural extracts as defined by (ii), the following natural extract mixture may be used.

In a first example, the natural extract mixture may have from about 0.1 wt% to about 99 wt% of hamamelitannin (Hamamelis virginiana) extract and from about 0.01 wt% to about 99 wt% of each of the following extracts: bearberry (Arctostaphylos uva ursi), bilberry (Vaccinium myrtillus), chlorella  
5 (Chlorella vulgaris), cowberry (Vaccinium vitis idaea), grape, molasses (Black sugar), mulberry, saxifraga and scutellaria. More preferably, the first example of the natural extract mixture is from about 5 wt% to about 30 wt% hamamelitannin extract, and from about 0.1 wt% to about 10 wt% of each of the following extracts: bearberry, bilberry, chlorella, cowberry,  
10 grape, molasses mulberry, saxifraga and scutellaria. Even more preferably, the first example of the natural extract mixture is from about 5 wt% to about 30 wt% hamamelitannin extract, and from about 0.1 wt% to about 10 wt% of each of the following extracts: bearberry, chlorella, grape, molasses mulberry, saxifraga and scutellaria.

15 A second example of the natural extract mixture is about 0.01 wt% to about 99 wt% pear extract, and from about 0.01 wt% to about 99 wt% guava extract. More preferably, the second example of the natural extract mixture has from about 0.1 wt% to about 10 wt% pear extract, and from about 0.1 wt% to about 10 wt% guava extract.

20 A third example of the natural extract mixture is from about 0.1 wt% to about 99.0 wt% of a mixture that has at least two of the following extracts: hamamelitannin, bearberry, bilberry, chlorella, cowberry, grape, molasses, mulberry, saxifraga or scutellaria.

A fourth example of the natural extract mixture has from about 0.1 wt% to about 99 wt% of hamamelitannin extract and from about 0.01 wt% to about 99 wt% of each of the following extracts: bearberry, grape, mulberry, saxifraga, and scutellaria. More preferably, the fourth example of the natural extract mixture is from about 5 wt% to about 30 wt% hamamelitannin extract, from about 0.1 wt% to about 10 wt% of each of the following extracts: bearberry, grape, mulberry, saxifraga and scutellaria.

The second component in all four embodiments of the present invention is an antioxidant. The antioxidant may comprise the following extracts: green tea, Rosemarinus officinalis (hereinafter "rosemary"), gamma oryzanol, a tocopherol or tocopherol derivative, or mixtures thereof. Although any one of the aforementioned antioxidants will exhibit activity when used individually, it is preferred that the antioxidant is at least two of the antioxidant extracts. It is most preferred that the antioxidant is a mixture of all four antioxidants. The total amount of antioxidant in the composition is from about 0.0001 wt% to about 50 wt%.

The green tea extract may be aqueous, alcoholic, glycolic, oil miscible powder, or a combination thereof. If the green tea extract is aqueous, alcoholic, or glycolic, then the green tea extract is from about 0.0001 wt% to about 30 wt% of the composition.

It is preferable that the green tea extract is a green tea extract powder in which the minimum of polyphenol content is about 65 wt% of the green tea extract powder, and that the polyphenol content comprises epicatechin gallate (ECG) and epigallocatechin gallate (EGCG). However,

other additional ingredients can be included in the polyphenol content.

When a green tea extract powder with the polyphenol content as defined above is used, the composition is from about 0.0001 wt% to about 5.0 wt% of the green tea extract powder and, more preferably, from about 0.0001  
5 wt% to about 1.0 wt% of the green tea extract powder.

The rosemary extract may also be aqueous, alcoholic, glycolic, oil miscible powder, or a combination thereof. The rosemary extract is from about 0.001 wt% to about 30 wt%. It is more preferable that an oil miscible rosemary extract is from about 92 wt% to about 98 wt% dry powder. When  
10 such an oil miscible rosemary extract powder is used, the composition is from about 0.001 wt% to about 15 wt% of the rosemary extract powder, and, more preferably, from about 0.05 wt% to about 5 wt% of the rosemary extract powder.

The antioxidant may also have from about 0.001 wt% to about 15  
15 wt%, preferably from about 0.01 wt% to about 5 wt%, gamma oryzanol. The antioxidant component further includes from about 0.01 wt% to about 10 wt%, preferably about 0.1 wt% to about 5 wt%, of a tocopherol or tocopherol derivative. Examples of suitable tocopherol derivatives are vitamin E acetate, vitamin E nicotinate and vitamin E linoleate.

20 In the second embodiment of the present invention, the skin whitening blend further includes an accelerant. The accelerant lactic acid aids in increasing the skin cell turnover rate, and thereby augments the skin whitening activity of the first embodiment of the present invention. Other suitable accelerants for use in the present invention are: glycolic

acid, a combination of glycolic and lactic acid, or a blend of malic acid, citric acid or lactic acid. In a first example, the accelerant is preferably lactic acid and is present from about 0.001 wt% to about 10 wt% of the composition. More preferably, the lactic acid is present from about 1 wt %  
5 to about 8 wt%. Most preferably, the lactic acid is present at about 2 wt%. In a second example, the accelerant is glycolic acid and is present from about 0.001 wt% to about 10 wt% of the composition. More preferably, the glycolic acid is present from about 1 wt % to about 8 wt%. Most preferably, the glycolic acid is present at about 2 wt%. As stated above, a  
10 combination of glycolic acid and lactic acid may be used. If the such a combination is used then the total weight percentage of the combination is from 0.001 wt% to about 10 wt%, more preferably from about 1 wt% to about 8 wt%, and most preferably about 2 wt%. In a fourth example, the accelerant is a blend of lactic acid, citric acid and malic acid (hereinafter  
15 "accelerant blend") and is present from about 0.01 wt% to about 10 wt%. More preferably, this accelerant blend is present from about 1 wt% to about 8 wt%. Most preferably, this accelerant blend is present at about 2 wt%.

The third embodiment of the skin whitening blend has the  
20 hypopigmenting component, the antioxidant, and further comprises a sunscreen. The sunscreen may be any sunscreen or any combination of two or more sunscreens, known in the art to be suitable for use in a topical composition. The sunscreen is from about 0.001 wt% to about 40 wt%, and more preferably from about 3 wt% to about 25 wt% of the composition.

Examples of suitable sunscreens and suitable concentrations thereof are as follows: from about 0.001 wt% to about 10 wt% ethylhexyl p-methoxy cinnamate (non-limiting examples of suitable ethylhexyl p-methoxy cinnamates are those available from the Givaudan Corporation

5 under the tradename "Parsol MCX", from Van Dyk Incorporation under the tradename "Escalol 557", from Haarman & Reimer Corporation under the tradename "Neo Heliopan Av", and from BASF under the tradename "Uvinul MC80"), from about 0.001 wt% to about 10 wt% oxybenzone or benzophenone-3 (non-limiting examples of suitable oxybenzones are those

10 available from ISP Van Dyk under the tradename "Escalol 567", from BASF under the tradename "Uvinul M40", from Neville Synthese Chem. Co./Rhone Poulenc (Rhodia, Inc.) under the tradename "Syntase 62", and from Rona/EM Ind. under the tradename "Eusolex 4360" product #605376), from about 0.001 wt% to about 10 wt% sulisobenzene, from

15 about 0.001 wt% to about 3.0 wt% dioxybenzone, from about 0.001 wt% to about 5 wt% of menthyl anthranilate, from about 0.001 wt% to about 25 wt% titanium dioxide, from about 0.001 wt% to about 20 wt% of zinc oxide, from about 0.001 wt% to about 10 wt% of a flavonoid or a derivative thereof, from about 0.001 to about 10 wt% butyl methoxydibenzoylmethane

20 (a non-limiting example of a suitable butyl methoxydibenzoylmethane is available from Roche Inc. under the trade name "Parsol-1789" product #64030), from about 0.001 wt% to about 10 wt% 4-isopropylidibenzoylmethane, from about 0.001 wt% to about 10 wt% octyl triazone, and from about 0.001 wt% to about 25 wt% of a sunscreen of methicone treated

titanium dioxide and zinc oxide that is manufactured by Miyoshi Kasei and distributed by U.S. Cosmetics under the tradename "TZ Powder type I(B)."

In one preferred embodiment, the sunscreen includes about 2 wt% ethylhexylmethoxycinnamate. In a second preferred embodiment, the  
5 sunscreen includes about 3 wt% ethylhexylmethoxycinnamate and about 1 wt% butyl methoxydibenzoylmethane. A third preferred sunscreen includes about 7.5 wt% ethylhexylmethoxycinnamate, about 2 wt% butyl methoxydibenzoylmethane and from about 3 wt% to about 4 wt% oxybenzone/benzophenone-3.

10 In the fourth preferred embodiment, the skin whitening blend has the hypopigmenting component, the antioxidant, the accelerant and the sunscreen. For the fourth embodiment, the parameters of each component are the same as set forth above.

The compositions of the present invention may incorporate one or  
15 more other ingredients such as, for example, an alcohol, a pH adjusting agent, chelating agent, emollient, emulsifier, film former, humectant, fragrance, masking agent, pigment, preservative, powder, surfactant, or a thickening agent.

The pH adjusting agent is preferably a base. The preferred bases  
20 are ammonium hydroxide, potassium hydroxide and sodium hydroxide. Potassium hydroxide and ammonium hydroxide are more preferred. Theoretically, other pH adjusting agents may be suitable for use in the present invention, if the pH adjusting agent both provides a stable

composition and adjusts the pH of the composition to a pH that suitable for topical use.

The preferred compositions of the present invention may have the following:

5

**EXAMPLE 1**

INGREDIENT	PERCENTAGE
Lactic Acid	2.0
Ammonium Hydroxide	0.001- 4.0
Humectants (e.g. Glycols, Glycerols)	0.5-15.0
Thickeners (e.g. Gums, Starches, Polymers)	0.1- 4.0
Chelants	0.001- 0.5
Emollients	1.0-10.0
Silicones	0.1-15.0
Preservatives	0.01- 2.0
Fatty Alcohols/Emulsifiers/Waxes/ Fatty Acids Alcohols	0.5-15.0 0-10.0
Vitamin E Acetate	1.0
Gamma Oryzanol	0.5
Rosemary Extract Powder	0.2
Licorice Extract (oil soluble powder)	0.05
Green Tea Extract Powder	0.0004- 1.00
Chlorella	0.1
Mulberry Extract Powder	0.1
Molasses	0.1
Uva Ursi Extract	1.0
Hamamelitannin Extract	10.0
Blend of Grape, Mulberry Root, and Scutellaria Root, Saxifraga Extracts	1.0
Ethylhexylmethoxycinnamate	0- 2.0
Demineralized Water	Q.S.

The following is another example of the present invention.

**EXAMPLE 2**

INGREDIENT	PERCENTAGE
Blend of Lactic Acid, Malic Acid, Citric Acid and Green Tea Extract	5.0
Ammonium Hydroxide	0.001-4.0
Humectants (e.g. Glycols, Glycerols)	0.5-15
Thickeners (e.g. Gums, Starches, Polymers)	0.1-4

Chelants	0.001-0.5
Emollients	1.0-10.0
Silicones	0.1-15
Preservatives	0.01-2.0
Fatty Alcohols/Emulsifiers/Waxes/Fatty Acids	
Alcohols	0.5-15
Gamma Oryzanol	0.2
Guava Extract	0.1
Licorice Extract (oil soluble powder)	0.05
Green Tea Polyphenols	0.0001
Pear Extract	0.1
Ethylhexylmethoxycinnamate	3.0
Butyl methoxydibenzoylmethane	1.0
Cyclomethicone-tetramer	5.0
Demineralized Water	Q.S.

Various modifications and alterations to the present invention may be appreciated based on a review of this application. These changes and additions are intended to be within the scope and the spirit of the present

5 invention as defined by the following claims.

What we claim is

1. A composition for whitening comprising:  
a hypopigmenting component; and  
5 an antioxidant.
2. The composition of claim 1, further comprising an accelerant  
that enhances skin cell turnover rate.
- 10 3. The composition of claim 2, further comprising a sunscreen.
4. The composition of claim 1, further comprising a sunscreen.
5. The composition of claim 1, wherein the hypopigmenting  
15 component is selected from the group consisting of
  - (a) a licorice extract;
  - (b) a natural extract that comprises at least one of the following  
extracts selected from the group consisting of: hamamelitannin, bearberry,  
bilberry, chlorella, cowberry, grape, guava, molasses, mulberry, pear,  
20 saxifraga and scutellaria; and
  - (c) a blend of the licorice extract and the natural extract.
6. The composition of claim 5, wherein the natural extract  
comprises a mixture of at least two extracts selected from the group

consisting of hamamelitannin, bearberry, bilberry, chlorella, cowberry, grape, guava, molasses, mulberry, pear, saxifraga and scutellaria.

7. The composition of claim 5, wherein the natural extract  
5 comprises a mixture of hamamelitannin, bearberry, chlorella, grape, molasses, mulberry, saxifraga, and scutellaria extracts.

8. The composition of claim 5, wherein the natural extract  
comprises a mixture of hamamelitannin, bearberry, bilberry, chlorella,  
10 cowberry, grape, molasses, mulberry, saxifraga and scutellaria extracts.

9. The composition of claim 5, wherein the natural extract  
comprises pear and guava extracts.

15 10. The composition of claim 1, wherein the hypopigmenting component is a licorice extract.

11. The composition of claim 10, wherein the licorice extract is  
selected from the group consisting of a water soluble licorice extract and  
20 an oil soluble licorice extract.

12. The composition of claim 11, wherein the licorice extract is a  
water soluble licorice extract in an amount from about 0.001 wt% to about  
30 wt% of the composition.

13. The composition of claim 11, wherein the licorice extract is an oil soluble licorice extract in an amount from about 0.001 wt% to about 5.0 wt% of the composition.

5

14. The composition of claim 13, wherein the oil soluble extract is in a powder form and is present in an amount from about 0.002 wt% to about 1.0 wt% of the composition.

10

15. The composition of claim 14, wherein the oil soluble extract is from about 0.05 wt% to about 0.1 wt% of the composition.

16. The composition of claim 1, wherein the hypopigmenting component is a combination of a licorice extract and a natural extract.

15

17. The composition of claim 1, wherein the hypopigmenting component is a mixture of natural extracts.

20

18. The composition of claim 17, wherein the natural extract mixture is from about 0.1 wt% to about 99.0 wt% of a mixture that has at least two of the following extracts: hamamelitannin, bearberry, bilberry, chlorella, cowberry, grape, molasses, mulberry, saxifraga, and scutellaria.

19. The composition of claim 1, wherein the antioxidant is selected from the group consisting of the following: green tea extract, rosemary extract, gamma oryzanol, a tocopherol or tocopherol derivative, and mixtures thereof.

5

20. The composition of claim 1, wherein the antioxidant comprises a green tea extract, a rosemary extract, gamma oryzanol, and a tocopherol or tocopherol derivative.

10

21. The composition of claim 20, wherein the antioxidant is from about 0.0001 wt% to about 50 wt% of the composition.

15

22. The composition of claim 2, wherein the accelerant is selected from the group consisting of: lactic acid; glycolic acid; a mixture of lactic acid and glycolic acid; and a blend of lactic acid, malic acid and citric acid.

20

23. The composition of claim 2, wherein the accelerant is lactic acid.

24. The composition of claim 23, wherein the lactic acid is from about 0.001 wt% to about 10 wt% of the composition.

25. The composition of claim 1, further comprising a vehicle.

26. The composition of claim 3, wherein the sunscreen is from about 0.001 wt% to about 40 wt% of the composition.

5 27. The composition of claim 3, wherein the sunscreen is selected from the group consisting of from about 0.001 wt% to about 10 wt% ethylhexyl p-methoxy cinnamate, from about 0.001 wt% to about 10 wt% oxybenzone or benzophenone-3, from about 0.001 wt% to about 10 wt% sulisobenzene, from about 0.001 wt% to about 3.0 wt% dioxybenzone,  
10 from about 0.001 wt% to about 5 wt% of menthyl anthranilate, from about 0.001 wt% to about 25 wt% titanium dioxide, from about 0.001 wt% to about 20 wt% of zinc oxide, from about 0.001 wt% to about 10 wt% of a flavonoid or a derivative thereof, from about 0.001 to about 10 wt% butyl methoxydibenzoylmethane, from about 0.001 wt% to about 10 wt% 4-  
15 isopropylidibenzoyl-methane, from about 0.001 wt% to about 10 wt% octyl triazone, and from about 0.001 wt% to about 25 wt% of a sunscreen of methicone treated titanium dioxide and zinc oxide.

28. The composition of claim 2, further comprising a pH adjusting  
20 agent.

29. The composition of claim 28, wherein the pH adjusting agent is a base.

30. The composition of claim 29, wherein the base is selected from the group consisting of ammonium hydroxide, potassium hydroxide and sodium hydroxide.

5 31. The composition of claim 1, further comprising an ingredient selected from the group consisting of an anti-inflammatory, an alcohol, a chelating agent, an emollient, an emulsifier, a film former, a humectant, a fragrance, a masking agent, a pigment, a preservative, a powder, a surfactant, and a thickening agent.

## INTERNATIONAL SEARCH REPORT

International application No.

PCT/US98/13600

**A. CLASSIFICATION OF SUBJECT MATTER**

IPC(6) : A61K 6/00

US CL : 424/401, 59; 514/844

According to International Patent Classification (IPC) or to both national classification and IPC

**B. FIELDS SEARCHED**

Minimum documentation searched (classification system followed by classification symbols)

U.S. : 424/401, 59; 514/844

Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched

Electronic data base consulted during the international search (name of data base and, where practicable, search terms used)

**C. DOCUMENTS CONSIDERED TO BE RELEVANT**

Category*	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
Y,P ---- A	US, 5,747,006 A (DORNOFF et al.) 05 May 1998, Abstract, column 1, line 52 to column 2, line 14, column 3, line 61 to column 5, line 5.	1, 2, 5-8, 10-13, 16-21, 25, 31 ----- 3, 4, 9, 14, 15, 22-24, 26-30



Further documents are listed in the continuation of Box C.



See patent family annex.

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Date of the actual completion of the international search

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